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11. SUPPLEMENTARY NOTES:

While much of the work that was discussed at the conference was eventually published, these publications were not commissioned under the auspices of the conference *per se*. However, there were two publications whose links to the conference were more direct, in that the experiments appeared in the journal *Molecular Diversity*. The editors of the journal attended the conference, and specifically commissioned the pieces at the conference:

Patten, P.A., Sonoda, T., and Davis, M.M. (1996). Directed evolution studies with combinatorial libraries of T4 lysozyme mutants. *Mol. Div.* **1**:97-108.

Lato, S.M. and Ellington, A.D. (1996). Screening chemical libraries for nucleic acid-binding drugs by in vitro selection: A test case with lividomycin. *Mol. Div.* **2**:103-110.

13. ABSTRACT:

The ONR provided funding for a conference that was designed to explore interactions between combinatorial methodologies in Biology and Chemistry. Breakthrough discoveries with replicating biopolymer libraries and chemical combinatorial libraries made the conference timely and allowed synergistic interactions to occur between the participants. For example, this conference was where David Bartel first reported on using a 'reflection selection' technique to identify nucleic acid aptamers that were stable to sera. Dr. Bartel's announcement was quickly picked up on by both academic and corporate scientists, and novel extensions of the work were informally discussed. Another goal of the conference was to begin to chart directions for the future, and to try to anticipate where these broad-ranging fields might be headed. Several of the talks, including the keynote address by Jack Szostak, made apparent how the science of combinatorial chemistry both provides insights into researches into the origins of life and molecular evolution, and ultimately supports more practical applications in industry. One participant, Jack Keene, said that despite a glut of industry conferences on the nuts-and-bolts aspects of combinatorial chemistry, that this was the best conference on the subject that he'd attended.

The Exploration of Sequence Space: Selecting Functional Molecules from Combinatorial Libraries

Indiana Molecular Biology Symposium IX
Presented by
The Indiana Institute for Molecular and Cellular Biology
October 12-15, 1995
Indiana Memorial Union

Thursday, October 12
Keynote Address

Jack Szostak	Massachusetts General Hospital

Friday, October 13
Session I. Replicating Biopolymer Libraries (Chair, Andrew Ellington)

Jamie Scott	Simon Frasier University
Carlos Barbas	The Scripps Research Institute
Lawrence Loeb	University of Washington School of Medicine
Jack Keene	Duke University Medical Center

Session II. Combinatorial Chemical Libraries (Chair, Jean Chmielewski)

Susan Freier	ISIS Pharmaceuticals, Inc.
William L. Scott	Lilly Research Laboratories
Anthony Czarnik	Parke-Davis
Michael Sofia	Transcell Technologies, Inc.
Bruce Eaton	NeXstar Pharmaceuticals, Inc.

Saturday, October 14
Session III. In Vitro Selection and Evolution of Catalysts (Chair, Norman Pace)

Gerald Joyce	The Scripps Research Institute
Donald Hilvert	The Scripps Research Institute
David Bartel	Whitehead Institute
Ton Schumacher	Whitehead Institute
Jean Chmielewski	Purdue University
Phillip Patten	University of California, Berkeley

Session IV. Drugs and Diagnostics (Chair, David Herron)

Richard Houghten	Houghten Pharmaceuticals, Inc.
Ronald Zuckerman	Chiron
Barry Polisky	NeXstar Pharmaceuticals, Inc.
Wilhelm P. Stemmer	Affymax

Sunday, October 15
Session V. Complexity and Life (Chair, William Roush)

Allan M. Ferguson	Tripos
Günter von Kiedrowski	Albert-Ludwigs-Universität
Gregory M. Fahy	Naval Medical Research Institute

The keynote address will begin at 7:45 pm on Thursday and will be followed by a reception/poster session until midnight. Plenary sessions are scheduled from 9:00-5:00 on Friday and Saturday, and from 9:00-noon on Sunday. A mixer/poster session is planned for Friday evening following the plenary talks, and a banquet will be held on Saturday evening. Presentations should last about 40 minutes including time for questions and discussion.

Attendance: 200

From NSF proposal:
Summary:

This proposal requests funds in partial support of a symposium to be held on the campus of Indiana University, Bloomington from October 12-15, 1995. The symposium is entitled **The Exploration of Sequence Space: Selecting Functional Molecules from Combinatorial Libraries.** This conference represents an acknowledgment of the fact that the interface between chemistry and biology has become increasingly integrated, and that scientists from both areas have begun to contribute to a new interdisciplinary field, combinatorial chemistry. Although combinatorial techniques are still in their infancy, they are nonetheless becoming increasingly important in exploring biological complexity and diversity, in understanding how chemical and biochemical self-organization can occur, and in the design and discovery of new drugs. The meeting is the ninth in an annual series presented under the auspices of the Indiana Institute for Molecular and Cellular Biology at Indiana University. Previous topics have included New Perspectives in Nucleic Acids, Crown Gall: Modification of the Plant Genome, The Genetic Analysis of Development, The Genetics and Molecular Biology of *Arabidopsis*, The Evolution of Genetic and Developmental Systems, Proteins as Machines, Biological Regulation by Protein Modification, and Origins and Evolution of Animal Bodyplans.

The objectives of the organizing committee are to bring together an international group of the leaders in disciplines that are contributing to the central theme of how combinatorial construction and evolutionary selection work together to mold biological and chemical structures. The invited speakers represent a diverse group of interests, including medicinal chemistry, nucleic acid and protein biochemistry, computer modelling, complexity theory, and nanotechnology. Many of these individuals have not interacted outside of the scope of this meeting, and previous experience has shown that an integrative conference of this kind can produce new syntheses in science. In particular, we have tried to balance the participation of industry and academic representatives, so that the science discussed is both fundamental and relevant. Given the exponential increase in the number of publications that are appearing on subjects relevant to this field, the timing is especially appropriate to achieve these kinds of interactions on this topic. Finally, we hope to increase intellectual interactions among students and faculty in different programs and departments at Indiana University. An effort is made to include graduate students and postdoctorals in the conference through reduced registration rates and by providing poster sessions with a focus on the work of younger scientists.

The conference will be announced in the scientific journals SCIENCE and CEN NEWS, and it will be advertised in a flier which will be distributed to university and industry scientists in the field of combinatorial chemistry.

Statement of Need:

It has long been known that the structures and functions of biological macromolecules have been molded by evolution. However, the development of new synthetic methods in chemistry and new amplification techniques in molecular biology have allowed the normally slow process of evolutionary optimization of molecular function to be accelerated by many orders of magnitude. As a result, numerous schemes have been devised for the selection of nucleic acids and proteins from random sequence libraries, and molecules with extremely novel functions have been readily isolated. Moreover, even molecules that cannot themselves be replicated, such as oligosaccharides or drugs such as the diazepams, have proven amenable to combinatorial synthesis and have accordingly been screened for modifications that potentiate new functions. Underlying all of these experimental probes of sequence, structure, and function is the notion that the interrelationships between different 'spaces' are being explored. Although the molecules are different, theorists are using the nascent data to determine how a sequence 'space' maps to structure 'space' and in turn to function or catalytic task 'spaces,' and commonalities in the pathways that are taken during the evolution of function are beginning to be discerned. The use of computer modelling has been of particular help in deciphering how molecules traverse these spaces. These topics can be most fruitfully discussed in an integrated fashion that ties together new results from several disciplines. Although existing meetings deal with some aspects of these subjects, no one meeting has attempted to fully integrate all of the approaches.

There is no organization devoted to jointly exploring chemical and biological diversity, and equivalent results cannot be obtained through existing society meetings.